NEUROKININ RECEPTOR ANTAGONISTS

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Mammalian tachykinins - substance P (SP), neurokinin A (NKA) and neurokinin B (NKB) - are widely distributed in peripheral tissues and in the central nervous system. Three types of distinct tachykinin receptors - NK_1, NK_2 and NK_3 - have been characterized up to now. The recent synthesis of selective non-peptide antagonists for these receptors has helped to investigate the physiological and pathological roles of tachykinins. CP 96,345, CP 99,994, RP 67,580 and RPR 100,893 have been described as NK1 receptor antagonists. SR 48,968 has been described as a NK_2 receptor antagonist, and SR 142,801 as a NK_3 receptor antagonist.

The involvement of NK_1 receptors in inflammation and associated sensory processing is supported by the ability of their antagonists to reduce plasma protein extravasation and edema triggered by a variety of experimental stimuli as well as the accompanying hyperalgesia. NK_1 receptors are also involved in the retching and vomiting reflex evoked by emetic agents. NK_2 receptors are preferentially involved in the non-adrenergic, non-cholinergic bronchoconstriction and cough response to irritants and allergens. Finally, only a few responses are elicited by NKB and selective agonists acting at the NK_3 receptor. Characterization of the physiopathological role of this receptor awaits further investigations using selective antagonists and under more relevant conditions.

In conclusion, tachykinins are important neuromodulatory agents whose involvement might be more important in chronic, remodelling processes than in acute responses.

Source: https://www.industrydocuments.ucsf.edu/docs/yqcb0000